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Trismus in head and neck oncology: a systematic review

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Summary The aim of this review was to identify systematically, criteria for trismus in head and neck cancer, the evidence for risk factors for trismus and the interventions to treat trismus. Three databases were searched (time period 1966 to June 2003) for the text “trismus” or “restricted mouth opening”. Included in the review were clinical studies (≥ 10 patients). Two observers independently assessed the papers identified. In 12 studies nine different criteria for trismus were found without justifying these criteria. Radiotherapy (follow-up: 6–12 months) involving the structures of the temporomandibular joint and or pterygoid muscles reduces mouth opening with 18% (sd: 17%). Exercises using a therabite device or tongue blades increase mouth opening significantly (no follow-up), effect sizes (ES) 2.6 and 1.5 respectively. Microcurrent electrotherapy (follow-up 3 months) and pentoxifylline (no follow-up) increases mouth opening significantly (ES for both: 0.3).
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Introduction

Trismus is a well known complication of head and neck cancer treatment.^{1,2} The prevalence of trismus after head and neck oncology treatment ranges from 5% to 38%.^{3,4} This large range in prevalence may be attributed to lack of uniform criteria, visual assessment of trismus and retro-

spective study design. Authors that do provide criteria for trismus do not explain why they define trismus in that specific way.^{3–6}

Risk factors for trismus in head and neck oncology have been described including tumours in the region of mouth closing muscles, radiation of the temporomandibular joint or the muscles of mastication, especially the medial pterygoid muscle but again retrospective research designs may flaw the conclusions of the studies.¹

Many case studies are published to illustrate treatment options for trismus.^{7–11} Also many reviews and or clinical guide lines are published how to prevent or treat trismus.^{1,12–16} However, the

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evidence supporting these prevention and treatment programs is usually not provided. Thus, until now the prevention and treatment of trismus seems to be based on clinical experience and good clinical practice.^{2,12,17}

Aim of this review was to identify systematically criteria for trismus, evidence for risk factors for trismus and interventions to treat trismus.

Methods

Literature databases, Medline, Embase, Cinhal were searched for "trismus" and "restricted mouth opening" in title, abstract and Mesh terms. Additionally in each database the free text words were combined with the data base specific Mesh term for "head and neck oncology" which includes the term "oral oncology". The time period over which was searched was 1966 to June 2003.

Included in this review were clinical studies with 10 or more patients written in Dutch, German and English. Excluded were non-systematic reviews, clinical recommendations concerning, surgical procedures, dental hygiene during oncology treatment or exercise programs, letters to the editor, case reports or case series ($n < 10$), studies not involving patients, studies not concerning head and neck oncology and papers written in other languages than the above mentioned.

All papers identified in the searches were retrieved from the library and were selected on the basis of the inclusion criteria by the first author (PD) after reading the abstract. The selected papers were copied and assessed independently by two observers (PD and WK) according to the criteria designed for this study. The following criteria were assessed,

1. prospective study (yes, no),
2. inclusion criteria described (yes, no),
3. percentages or numbers of men and women included in the study reported (yes, no),
4. descriptive statistics, mean and sd, or median and inter quartile range, for age reported (yes, no),
5. location of tumour reported with sufficient detail, for instance floor of the mouth, tongue, salivary glands etc. oropharyngeal or oral cavity tumour is not detailed enough (yes, no),
6. baseline assessment of mouth opening (yes, no),
7. criteria for trismus described (yes, no),
8. trismus described in subjective terms, for instance patients experience stiffness during mouth opening or patients experience a restricted mouth opening during eating (yes, no),

9. trismus measured (yes, no),
10. measurement instrument described (yes, no),
11. repeated measurements performed to increase reliability (yes, no),
12. percentage or number of patients with trismus described (yes, no),
13. number of patients included in the study ($10 \leq 29$, $30 \leq 99$, 100 or more),
14. number of patients assessed for trismus ($10 \leq 29$, $30 \leq 99$, 100 or more).

The assessments of both observers were entered in a database and Cohen's κ was calculated for dichotomous data (criteria 1–12) and a linear weighted κ was calculated for ordinal data (criteria 13 and 14). A consensus meeting was held between the two observers to discuss discrepancies in assessment. Consensus was reached by means discussion if no consensus could be reached the assessment of the third author (JR) would be binding.

Results

A total of 203 papers were identified in the databases. (References available on request at the corresponding author.) Of these papers, 24 were excluded because they were written in a foreign language not understandable for the authors. Of the remaining 179 papers the majority of papers were clinical studies ($n = 77$). The two observers assessed these papers. During the assessment process 11 additional papers were excluded because they involved a survey among hospitals about treatment regimes for head and neck oncology patients, intubation procedures, reconstructive surgery, trauma or trismus was not evaluated (Table 1) (Appendix A: list of selected papers).

For the inter observer agreement of dichotomous data Cohen's κ was 0.79 and for ordinal data a linear weighted κ was 0.88. One paper was only assessed by the first author because it was identified after the consensus meeting.

The number and percentages of papers meeting the different criteria are presented in Table 2. When the scores of the criteria 1–12 are summed, the mean sum score is 5.5 (sd: 1.6) the median sum score is 5.0 (inter quartile range: 5–6.3). Sixteen papers (24%) of the papers had a sum score of 7 or more. In 12 studies nine different criteria for trismus were found (Table 3). Some authors defined trismus dichotomously as a mouth opening less than 40 mm where as other authors defined trismus as a mouth opening less than 20 mm. Three authors

Table 1 Types of publications found in the search

Publications	Excluded % (n)	Included % (n)
Publications in other languages ^a	11.8% (24)	
Bulgarian	1	
Chinese	3	
French	8	
Greek	2	
Hungarian	1	
Italian	3	
Japanese	2	
Polish	1	
Portuguese	2	
Turkish	1	
<i>Publication type</i>		
Case study or case series involving <10 patients	26.6% (54)	
Clinical recommendation	15.8% (32)	
Review	4.4% (9)	
Systematic review	—	
Letter	3.4% (7)	
Clinical study involving ≥ 10 patients 37.9% (77)		
Relevant for the review		32.5% (66)
Not relevant	3.6% (11)	
Survey of hospitals	1	
Intubation procedure	1	
Reconstructive surgery	2	
Trismus not evaluated	6	
Trauma	1	
Total	67.5% (137)	32.5% (66)

^a Papers published in other languages than English, German or Dutch.

Table 2 Percentage and number of publications fulfilling assessment criteria

Assessment criteria	% (n)
Prospective study	27% (18)
Inclusion criteria of the study described	95% (63)
Percentages or numbers of men and women reported	80% (53)
Descriptive statistics for age reported	12% (8)
Location of tumour reported with sufficient detail	94% (62)
Baseline assessment of mouth opening	20% (13)
Criteria for trismus described	18% (12)
Trismus described in subjective terms	15% (10)
Trismus measured	12% (8)
Measurement instrument described	5% (3)
Repeated measurements performed	2% (1)
Percentage or number of patients with trismus described	86% (57)
<i>Number of patients included in the study^a</i>	
10—≤ 29	29% (22)
30—≤ 99	46% (30)
100 or more	26% (17)
<i>Number of patients assessed for trismus</i>	
10—≤ 29	33% (22)
30—≤ 29	46% (30)
100 or more	21% (14)

^a Due to rounding off the percentages exceed 100%.

Table 3 Criteria^a for trismus according to different authors

Authors	Mouth opening (mm)	Lateral movements
Nguyen et al. (1988) ²⁷	<40	—
Steelman and Sokol (1986) ^{b4}	<35	—
Ichimura and Tanaka (1993) ²⁸	<35	—
Teo et al. (2000) ²⁹	<30	—
Chua et al. (2001) ¹⁹	<25	—
Footte et al. (1990) [minimal trismus] ³⁰	20–30	—
Teo et al. (1998) ³¹	<20	—
Chang et al. (2000) [severe trismus] ³²	<20	—
Jen et al. (2002) ⁶	<20	—
Sakai et al. (1988) ⁵		
Normal	<30	—
Moderately restricted	20–30	—
Severely restricted	<10	—
Thomas et al. (1988) ³		
Light	>30	—
Moderate	15–30	—
Severe	<15	—
Bertrand et al. (2000) ^{c33}		
Grade 1	>40	Difference < 25%
Grade 2	>30	Difference > 25%
Grade 3	<25	No lateral movements

^a Criteria are literally reproduced from the text.

^b Steelman citing Gelb (1977).³⁴ However, in that book no justification is provided for this criterion.

^c Criteria for vertical as well as horizontal movements should be fulfilled.

define trismus according to a more gradual scale of which one also includes horizontal movements. None of these studies provided justification for these criteria.

Papers were selected for detailed review if they met three assessment criteria; prospective study design, base line assessment of trismus and measurement of trismus.

Four papers fulfilled these criteria (Table 4).^{18–21} The assessment scores of these papers ranged from 6 to 11 points. Two cohort studies evaluated the effects of Microcurrent therapy and Pentoxifylline on mouth opening. One RCT analysed the effects of different exercise programmes on mouth opening. Finally one cohort study analysed the effects of radiotherapy on mouth opening. To compare effects of the interventions effect sizes (ES) were calculated:

$$ES = \text{mean}_{\text{change}} / \text{sd}_{\text{pretreatment}}$$

Exercises using a therabite device or tongblades increase mouth opening significantly (no follow-up), effect sizes (ES) 1.5 and 2.6 respectively. Pentoxifylline (no follow-up) and Microcurrent therapy (follow-up: 3 months) increase mouth significantly. Effect size of both interventions was 0.3. Radiotherapy involving the structures of the TMJ and or pterygoid muscles reduces mouth

opening with 18% (sd: 17%) (follow-up: 6–12 months). For an overview of the finding see Table 4.

In a posthoc analysis the English abstracts or titles were analysed of the papers that were excluded because of the language they were written in. Of the 24 papers there were three case studies, four clinical recommendations or reviews, four clinical studies of which one was retrospective, and of nine publications the abstracts were not available in the data bases. Three did not have trismus as a topic of study and one publication was similar to an English publication of the same author, judged on the basis of the abstract. Thus at the most 12 publications, three clinical studies and nine papers of which the English abstracts were not available in the data bases, might have been reviewed in this study also.

Discussion

Of all papers about trismus only 37% (66/179) were clinical studies and were evaluated systematically. The overall quality of papers reviewed was moderate to poor. Only 24% of the papers had

Table 4 Overview of the studies and their results

Author	Study type	Intervention/dosage	Included <i>n</i> , inclusion criteria	Evaluated	Follow-up	Outcome in mm, mean change (sd)	95%CI	ES
Buchbinder et al. (1993) ²⁰	RCT	10 exercise sessions per day, over 10 weeks	21, mouth opening ≤ 30 mm, radiation completed <5 years	21	—			
		Therabite				13.6 (6.6)	8.6 to 18.7	2.6
		Tongblades				6.0 (2.6)	3.6 to 8.4	1.5
		Forced opening				5.4 (4.4)	−0.05 to 10.9	1.1
Chua et al. (2001) ¹⁹	Cohort	8 weeks Pentoxifylline/ 400 mg 3 times daily	20, mouth opening ≤ 25 mm, radiation completed ≥ 6 months	16	—	4.0 (6.3)	0.6 to 7.4	0.3
Lennox et al. (2002) ¹⁸	Cohort	Microcurrent therapy/ 10 treatments in 5 days	26, detectable fibrosis	23	3 months	2.6 (2.4)	0.1 to 3.6	0.3
Goldstein et al. (1999) ²¹	Cohort	Radiotherapy	58, head and neck oncology	58	6–12 months	−18% (17%)		

ES: effect size was calculated as $\text{mean}_{\text{change}} / \text{sd}_{\text{pretreatment}}$.

a sum score of more than half of the maximal score. When three selection criteria (1, 6, and 9) were applied only four studies fulfilled these criteria.

Assessment criteria

For systematic reviews analysing randomised clinical trials, assessment criteria lists are available.²² We did not use these lists because we were not only interested in RCTs but also in prognostic research and cohort studies (observational studies). The criteria list used was based on basic requirements of research methodology and statistical description of the population under study.

To assess risk factors and treatment strategies, studies should at least be prospective because otherwise several forms of bias (selection bias and information bias) may be introduced in the study. One of the principal requirements of a study is that inclusion criteria are described. Additionally, the study population should be described with sufficient detail using adequate statistics. These adequate statistics enable data pooling in case of meta-analysis. Many studies describe the study population with respect to age according to mean and range, however, these statistics are inadequate for data pooling and, thus, should be replaced by mean and standard deviation or median and inter quartile range.²³ If risk factors for trismus are to be analysed, sufficient detail should be provided with respect to location of the tumour. "Oropharyngeal tumour" or "tumour of the oral cavity" tumour is not detailed enough. A tumour of the buccal mucosa or cancer of the anterior floor of the mouth may not lead to trismus at all, whereas a tumour of the retromolar region may have a high risk for inducing trismus, despite this they are both tumours of the oral cavity. For evaluation of risk factors for trismus or treatment effectiveness, base line assessment of trismus is required. Because no gold standard exists as to which amount of mouth opening should be regarded as trismus, criteria for trismus were assessed. It appeared that a wide range of criteria was used without documenting why these specific criteria were used. It is unclear when a restricted mouth opening results in functional limitations such as problems with biting, chewing, yawning, etc. To overcome this dilemma trismus might be assessed in subjective terms such as "Does your mouth opening feel restricted" or "Are you limited in eating because of your mouth opening". Only 10 studies described trismus subjectively.

For adequate evaluation of trismus, mouth opening should be measured, because visual assessment of mouth opening is highly inaccurate and leads to discrepancies between the assessed mouth opening and the actual mouth opening. For a reliable assessment of mouth opening, repeated measurements should be performed.²⁴

To obtain a rough estimation of the power of the study and the drop out rates, the numbers of patients included and evaluated for trismus were assessed.

Excluded studies

Cases studies were not included in this review because they are highly susceptible for selection bias and case studies are more or less anecdotal. They serve either to illustrate a rare case, a rare complication or a new treatment strategy. Case studies and case series may be interesting from a clinical point of view but from a statistical point of view case series and case studies lack power. As cut off point for inclusion ≥ 10 patients chosen for reasons explained previously.²⁵ Expert reviews were excluded because it is unclear which sources of information (databases) were used to identify relevant papers and how these papers were selected and how these papers were critically assessed.²⁶ The same principles apply to the clinical recommendations.

By restricting our review to papers written in English, German and Dutch we introduced a selection (language) bias. Which consequence this type of bias has is not clear for the outcome of this review. At the most 12 publications were excluded from this review because of the language bias. If these papers have a similar methodological quality as the papers included in this review only 6% (4/66) would have been selected for the detailed review (prospective study design, base line assessment of trismus and measurement of trismus). This may resulted in one additional study in the detailed review.

Final selection of the studies

The final selection according to the three criteria (prospective study design, base line assessment of trismus and measurement of trismus) was performed for several reasons. If risk factors for trismus are to be identified one has to know whether trismus was absent before the exposure to the risk factors (surgery and or radiotherapy) and in which percentage of the patients at risk actually

developed trismus after the exposure. These requirements can only be fulfilled in a prospective study. For the selection of papers describing therapeutic effects the previously mentioned requirements must be met. Therefore it was not possible to identify risk factors in the majority of studies.

Exercises using a therabite device or tongblades significantly increase mouth opening on short term, the effect sizes were large. Pentoxifylline increased mouth opening on short term and electrotherapy increases mouth opening (follow-up: 3 months) but the effect sizes are small. Radiotherapy involving the structures of the TMJ and or pterygoid muscles reduces mouth opening with 18% (sd: 17%).

The effect size relates the mean change as a result of the exposure to the variance within the population before the exposure. A large effect size indicates that the mean change is large relative to the variance before the exposure.

Conclusion

Overall, trismus is usually not investigated primarily but as a secondary outcome variable. In general the quality of the studies analysed was moderate. Despite the numerous papers written the knowledge about trismus remains scarce. Only four papers fulfilled three basic requirements. Effects of therapeutic interventions are scarcely investigated. The effect sizes range from small to large but the RCT with large effect sizes does not have a follow-up. Research into criteria for trismus, functional consequences of trismus, risk factors for trismus and interventions studies are needed.

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A complete list of the papers retrieved from the data bases is available from the corresponding author.

Appendix A

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